The term “mixed dementia” refers to the coexistence of more than one possible cause of dementia in a given patient and has been subjected to much controversy in the past literature. Practically, “mixed dementia” usually refers to the coexistence of Alzheimer’s disease (AD) with a vascular contribution. It is a commonly used clinical diagnosis although published guidelines lack consensus on a clear definition. The National Institute of Neurological Disorders and Stroke–Association Internationale pour la Recherche et l’Enseignement en Neurosciences (NINDS-AIREN) diagnostic criteria for vascular dementia did not include a definition for “mixed dementia,” and proposed the use of the term AD with cerebrovascular disease. In the Alzheimer’s Disease Diagnostic Treatment Center criteria, “mixed dementia” is defined as a condition in which there is evidence of vascular disease with the coexistence of one or more disorders that may be causally related to the dementia. In the most recent statement on Vascular Contributions to Cognitive Impairment and Dementia, the term Vascular Cognitive Impairment (VCI) represents the whole spectrum of cognitive impairment associated with vascular brain injury including coexistent AD. The term “mixed dementia” is not used or defined even though authors mention that the neuropsychological diagnosis of VCI is “complicated by the difficulty of clinically differentiating Alzheimer disease or VCI from mixed (Alzheimer disease plus cerebrovascular disease) disease, which may be more common than either “pure” Alzheimer disease or “pure” VCI.”

The Canadian Cohort Study of Cognitive Impairment and Related Dementias (ACCORD) study, evaluated the distribution of clinical diagnoses of patients referred to Canadian memory disorders clinics between 1997 and 1999. This study including 1136 subjects showed that 59% had dementia 47.2% of which were due to Alzheimer’s Disease, and 27.5% were mixed (AD with another diagnosis). In the Cardiovascular Health Study, a community-based study, 33% of dementia cases were due to AD with a vascular contribution. Clinico-pathological studies of individuals with dementia show that “mixed dementia” is even more prevalent. For example, the Medical Research Council Cognitive Function and Ageing Study (MRC CFAS), a community-based study of elderly individuals showed that 61% of dementia cases displayed AD pathology and 54% displayed vascular pathology and most cases had mixed pathology at autopsy. In the Rush Memorial and Aging Project, 50% of dementia cases had mixed disease on neuropathological examination. Few studies have made clinico-pathological correlations in the setting of specialized memory disorders clinics or in clinical trials of AD.

In this issue of the Canadian Journal of Neurological Sciences, Wang et al describe the neuropathological findings of 16 individuals with a clinical diagnosis of AD who were also enrolled in clinical trials. Five of these patients (31%) had pure AD pathology, ten had mixed pathology (AD with contribution from another condition, most commonly vascular in nature) and only one patient had non-AD pathology. Individuals with mixed AD had poorer performance on the baseline Functional Rating Scale (FRS) in problem-solving and community affairs. The good news from this study is that 94% (15 out of 16 cases) were correctly diagnosed with AD, validating the expertise of this specialized memory disorders clinic. The bad news is that most cases of AD were mixed, and this was not recognized clinically despite a thorough clinical evaluation including the use of neuroimaging. In fact, neuroimaging showed white matter abnormalities in only four out of the ten patients with comorbid vascular neuropathology.

Clinically, this study reiterates that a significant proportion of AD cases are “mixed” in nature and this is even truer in older cohorts and in community samples. The most
common concomitant condition being vascular, this opens the door to possible preventive interventions. There are no clinical trials targeting vascular risk factors in individuals with overt dementia. Nevertheless, a retrospective study in a memory disorders clinic showed that individuals with a diagnosis of AD progressed significantly more slowly when most of their vascular risk factors were treated. These findings underscore the importance of optimal control of vascular risk factors in individuals with dementia.

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